

Effect of a Dietary Intervention on Autistic Behavior

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Autistic syndromes are characterized by impaired social, communicative, and imaginative skills. Urinary peptide abnormalities, in part due to gluten and casein, have been detected in some individuals with autism. These abnormalities reflect processes with opioid effect, which may explain the behavioral abnormalities seen in autism. The aim of this single-blind, controlled study was to evaluate the effect of a gluten-free and casein-free diet for children with autism and urinary peptide abnormalities. Observations and tests were carried out with the 20 participating children before they were randomly assigned to either the diet or the control group. The experimental period was 1 year, after which observations and tests were repeated. Significant reduction of autistic behavior was registered for participants in the diet group, but not for those in the control group.

Although autism may have been observed in ancient Mesopotamia (Gillberg & Coleman, 2000), autistic syndromes were first reported medically only 60 years ago (Asperger, 1944; Kanner, 1943). Autistic syndromes are characterized by a combination of impaired social, communicative, and imaginative skills. Furthermore, restricted and repetitive patterns of behavior with a variety of routines and rituals are common (American Psychiatric Association, 1994). A strong genetic influence has been detected in the disorders (e.g., Bailey et al., 1995), and various biological as well as cognitive abnormalities have been reported (e.g., Gillberg & Coleman, 2000).

Urinary peptide abnormalities, consisting of abnormal patterns and elevated levels of peptides, are biological abnormalities that were first reported in individuals with autism 20 years ago (K. L. Reichelt et al., 1981), and the original

findings have been replicated repeatedly (Cade et al., 1999; Israngkun, Newman, & Patel, 1986; K. L. Reichelt, Sælid, Lindback, & Bøler, 1986; Remme, Koetzer, Haugland, Reichelt, & Brønstad, 2001; Shanahan, Venturini, Daiss, & Friedman, 2000; P. Shattock, Kennedy, Rowell, & Berney, 1990). Urinary peptide abnormalities are in part derived from gluten, gliadin, and casein. Gluten and gliadin are found in the most common grains and cereals, and casein is found in milk and milk products. Elevated levels of peptides indicate insufficient breakdown of the proteins and may be the result of genetically based peptidase deficiencies (Reichelt, Knivsberg, Lind, & Nødland, 1991). High levels of these peptides also indicate that the abnormalities are due to an external source (i.e., food containing the proteins in question; P. Shattock et al., 1990).

Positive results of dietary interventions have been reported from surveys

(Klaveness & Bigam, 2002; Rimland, 1988; 2000; P. Shattock, 1995) and case studies (Adams & Conn, 1997; Knivsberg, Reichelt, & Nødland, 1999), as well as from studies of groups of children with autism (Cade et al., 1999; Knivsberg, Reichelt, Nødland, & Høien 1995; Knivsberg, Wiig, Lind, Nødland, & Reichelt, 1990; Lucarelli et al., 1995; Reichelt, Ekrem, & Scott, 1990; Whiteley, Rodgers, Savery, & Shattock, 1999). The beneficial effects of gluten-free and casein-free diets have also been reported by mothers (Lewis, 1998; McKelvey, 1997; Neale, 1997; Scott, 1998; Seroussi, 2000), and even by a 12-year-old boy (Jackson, 2002). To our knowledge, though, the effect of excluding gluten and/or casein from the diet of children with autism has not been evaluated in a controlled, randomized study with an intervention period of 1 year, as has been done in the present study.

The rationale for implementing dietary intervention is that the peptides from gluten and casein reflect processes with opioid effect (e.g., P. Shattock & Whiteley, 2002; Wakefield, Puleston, Montgomery, Anthony, O'Leary, & Murch, 2002). The opioid peptides in question, especially monoamines, must modulate transmitter systems (P. Shattock et al., 1990), and unusual effects on transmitter systems may explain a variety of the behavioral abnormalities of individuals with autism (P. Shattock et al., 1990). Serotonin influences sleep as well

as arousal, anxiety, affect, learning, memory, thermoregulation, motor control, pain modulation, and aggression (Wilkinson & Dourish, 1991). Increased uptake of serotonin to blood platelets has been reported by several researchers (for review see Gillberg & Coleman, 2000), and a peptide that stimulates serotonin uptake has been identified (Pedersen, Ying, & Reichelt, 1999; K. L. Reichelt, Knivsberg, Nødland, & Lind, 1994). Furthermore, dopamine influences motor control as well as attention and hyperactivity, whereas noradrenaline is linked to functions like sleep, arousal, emotions, and selective attention (Ciaranello et al., 1995). The opioids in question increase dopamine activity (Hole et al., 1979), and opioids are linked to stress responses, affective processes, and reward mechanisms (Ciaranello et al., 1995).

The goal of the present study was to evaluate the effects of a gluten-free and casein-free diet for children with autism and urinary peptide abnormalities. Twenty children were matched pair-wise according to age, cognitive level, and severity of autistic behavior. One child in each of the 10 pairs was then randomly assigned to the diet group. The other 10 children formed the control group, a nondiet group. The participants' behavior was registered before and after the experimental period of 1 year. The registrations covered communicative aspects, reciprocal social interactions, emotions, learning, play behavior, and movements. We hypothesized that we would register a decrease of autistic traits in the diet group but not in the control group.

Method

Design

To compare the diet group and the control group, we chose a single-blind controlled design, which has been used in dietary interventions for rheumatoid arthritis (e.g., Kjeldsen-Kragh et al., 1991). Deterioration, reduction of acquired skills, and increase of autistic behavior have been reported after reintroduction of gluten and/or casein to children who have been abstaining from these for

shorter or longer periods (Knivsberg et al., 1995; Lucarelli et al., 1995; R. Shattock, 1995; Whiteley et al., 1999). We therefore found it difficult and unethical to use a double-blind crossover design, which otherwise seems ideal for a study of this kind.

To overcome the heterogeneity of autism, the participating children were matched pair-wise and then randomly assigned to a group. Given the prevalence of autism, we considered age, cognitive level, and severity of autistic traits to be the most important variables in pairing the children. Gender was not reported, as information related to this variable is rarely reported in studies about autism.

The autistic behavior of the participants is the focus for this report. To assess the children's autistic behavior, we relied on an observation scheme, the DIPAB (*Diagnose of Psykotisk Adferd hos Børn* [Diagnosis of Psychotic Behavior in Children; Haracopos & Kelstrup, 1975a]) and parent reports. According to Gillberg (1995), mothers are very reliable informants of their children's development, for normal, adequate behavior as well as for deviant behavior. The children participated in a larger study in which a cognitive test (Leiter, 1979), linguistic tests (Gjessing et al., 1975; Hagtvet & Lillestølen, 1985), and a motor assessment (Henderson & Sugden, 1992) were also used before and after the experimental period of 1 year. Reports were thereafter written on each individual's development (for detailed results from these tests and reports, see Knivsberg, Reichelt, Høien, & Nødland, 2002).

Participants

All the participants had been diagnosed with autism by professionals in the field of child psychiatry/neurology who were not connected to the current project. The children also had urinary peptide abnormalities. Mean age was 7 years 6 months ($SD = 1.8$ yrs) for the 10 children in the diet group and 7 years 2 months ($SD = 1.9$ yrs) for the 10 children in the control group.

We used the DIPAB to assess the severity of autistic behavior before the

children were matched pair-wise. A child's total impairment consists of scores related to resistance to social interaction and scores for strange or unusual behavior. The diet group initially had a total impairment score mean of 12.5 ($SD = 2.2$). The mean in the control group was 11.5 ($SD = 3.9$). The mean of the non-verbal cognitive level, measured with *Leiter International Performance Scale* (Leiter, 1979), had to be based on test scores from nine children in each group, as one pair of girls did not respond properly to the tasks presented. The mean for the children in the diet group was 81.0 ($SD = 36$) and, for the children in the control group, 84.6 ($SD = 37$).

Materials

The DIPAB is a Danish scheme that was standardized on 392 children. The scheme has two main parts. The first part is designed for registration of a child's skills and general level of function. The second part contains 18 questions regarding autistic behavior, displayed in Figure 1. For this study, the first 17 were used. From these questions, information about participants' social isolation and bizarre behavior is revealed. According to Haracopos and Kelstrup (1975b), the last question, regarding specific skills a child may master, must be treated separately.

Haracopos and Kelstrup (1975b) underlined that different observers may evaluate behavior differently and that a child may behave differently in different settings. So that the scores will be as objective as possible, each question is thoroughly explained and examples of each behavior are given. Question 1 may serve as an example (for simplicity the male or female child is referred to as "he"). The question is, Does the child use verbal communication? The authors explain this question with the following questions: How willingly does the child communicate? How willingly does he talk about himself, about his experiences and interests? How willingly or eagerly does the child ask questions to satisfy his curiosity and learn something new about his surroundings or other people? After this

explanation, the authors present the following examples of verbal communication:

- The child communicates his own *experiences*—that he has been to the zoo, has had his birthday, has been home for a weekend visit, has been for a walk in the woods, or other similar experiences.
- The child communicates his *interests*—tells about his truck or other toys, about a sketch he has made, about an airplane he wants to build, and so forth.
- the child communicates his *expectations*—that he is looking forward to Christmas or his birthday, that he is looking forward to trying the slide, going to the amusement park, having some sweets, visiting grandma, and so forth.
- the child expresses *curiosity*—asks questions about how things are constructed, how to make a fire engine, how to play ludo or chess, asks where the cookie jar has been hidden, and so forth.

The authors further explained that it is not fluency, accuracy, or speech impairment that is to be registered, but the eagerness with which the child uses verbal communication.

The questions are rated on a 5-point scale, where 1 = *normal behavior* (e.g., the child communicates as other developmentally matched children do), 2 = *somewhat deviant behavior* (e.g., the child sometimes talks to an adult but may need the adult to assist him or her with communication by asking specific questions), 3 = *clearly deviant behavior* (e.g., the child is not assisted by leading questions and seldom talks to an adult), and 4 = *extremely deviant behavior* (e.g., the child almost never addresses an adult). A score of 0 means that the question cannot be evaluated (e.g., the child does not have verbal language abilities). Based on a combination of the questions, a child's social interaction or isolation and a child's bizarre or unusual behavior is computed (Haracopos & Kelstrup, 1975a). Consistency of the results has been demon-

1. Does the child use verbal communication?
2. Is the child's verbal communication compulsive or stereotypic?
3. Does the child engage in echolalia?
4. Does the child use non-verbal communication?
5. How does the child react when spoken to?
6. Does the child resist learning?
7. Does the child share his/her feelings with others?
8. Does the child resist physical contact?
9. Does the child depend on the presence of an adult?
10. How is the child's eye contact?
11. How is the child's contact with other children?
12. Does the child show strange emotional reactions?
13. Does the child express abnormal anxiety?
14. Does the child demand that the environment is totally stable or unchangeable?
15. Does the child use toys and playing material in a strange way or without purpose?
16. Does the child have an attachment/affinity for a specific item?
17. Does the child have unusual movements?
18. Does the child have extraordinary abilities or talents?

FIGURE 1. DIPAB questions about specific autistic behavior. *Note.* From *Diagnose of Psykotisk Adfærd hos Børn Observationsskema* [Diagnosis of Psychotic Behavior in Children Observation Scheme], by D. Haracopos and A. Kelstrup, 1975. Herning, Denmark: Special-Pædagogisk Forlag A/S. Copyright 1975 by Special Pædagogisk Forlag A/S. Reprinted with permission.

strated through item analyses of the questions that were conducted when the scheme was standardized (Haracopos & Kelstrup, 1975b).

The cognitive assessment was conducted with the *Leiter International Performance Scale*, a nonverbal intelligence test used for children with language disorders, attention-deficit/hyperactivity disorder, and autism and other developmental disorders. The test is standardized for 2- to 18-year-olds. Normal mean is 100 points, and standard deviation is 16. The test material consists of approximately 200 wooden, 1-inch cubical blocks, a response frame with slots, and paper stimulus strips. The test uses number, perceptual, and abstract reasoning tasks. The tasks are presented on the wooden frame and demonstrated by the test leader without words. The child does not have to look directly at the test leader or utter a word to answer; he or she only has to move blocks into their appropriate slots to demonstrate understanding of the concept being measured.

Procedure

The Regional Committee for Scientific Ethics and the Data Inspectorate ap-

proved this study. Information on the study was thereafter distributed through journals and through the school psychological service, and parents contacted the project leader (the first author) for further written and oral information. Participation was based on written consent, but parents could withdraw their children from the study whenever they wanted. All parents accepted that their child would be assigned randomly to either the diet group or the control group.

Urine analyses were completed anonymously; that is, each child was given a code number and code name. The urine samples were cleaned to separate peptides and other similarly sized molecules from smaller and larger molecules. The peptide fraction was then injected onto a column and a solvent passed along the column. This process is known as a *gradient elution high performance liquid chromatography* (HPLC; for detailed information about this method, see W. H. Reichelt & Reichelt, 1997).

Information regarding each child's autistic traits, cognitive level, and language and motor skills was collected through structured interviews and tests. The project leader met parents and children in their homes, where parents were

interviewed using the DIPAB. Because children with autism habituate slowly (Bernal & Miller, 1970), the children's skills and abilities were formally tested in the school or in the kindergarten the children attended. The testing was carried out in the same room and at the same time of day that the children usually had special one-on-one training. To minimize the stress for the children as much as possible, the children's special educator or special assistant was asked to be present during the testing. We assumed it would be positive for each child to have a familiar adult at his or her side.

The project leader then matched the children pair-wise according to age, cognitive level, and severity of autistic symptoms. Professionals outside the project randomly assigned children to the diet group or the control group. A dietician visited the parents of the children in the diet group and gave the parents oral and written information about gluten-free and casein-free diets. The parents were free to contact the dietician by phone during the experimental period, but no formal monitoring of the dietary compliance was carried out.

All parents had monthly telephone contact with special educators familiar with autism and the project. Both groups of parents were contacted to give all received the same kind of contact, attention, and opportunity to discuss problems related to raising a child with autism. Because the children lived in different areas of the county, their special education

programs or other interventions could not be monitored or evaluated.

The data-collection procedure was repeated after 1 year; however, this time the interviews with the parents were conducted after the formal testing had been carried out. The project leader had no contact with the families during the experimental period and did not know which children belonged to which group until the formal testing and interviews had been repeated.

Statistics

Both repeated measures within the two groups of children and between the two groups were compared. For this mixed factorial experiment, nonparametric tests were used instead of analyses of covariance, because the measures were not normally distributed. The tests are considered to be both conservative and strict, and significant changes in a small group are strongly indicative of the effectiveness of the intervention. The two-tailed Wilcoxon test for related samples was used to compare the development within the two groups, and the two-tailed Mann Whitney U test for unrelated samples was used to compare the development between the two groups. The Mann Whitney U test was chosen because the children in the two groups, although pair-wise matched, might differ from each other on other measures and influence. The statistical program used was SPSS for Windows.

Results

The DIPAB was constructed to give information on two main characteristics of autism: social isolation and strange or bizarre behavior. Social isolation is calculated from a child's communicative abilities, what a child actually masters, and information on resistance to communication. Both the latter aspects and the main information on social isolation and bizarre behavior can be derived from the scheme. For Child 2 in the diet group and Child 12 in the control group, Questions 1, 2, and 3 could not be answered and were consequently registered as missing.

A child's abilities to communicate and interact (K-scores) are computed from the scores for verbal and nonverbal communication, reaction when spoken to, resistance to learning, sharing of feelings, reactions to physical contact, eye contact, peer relationship, and handling of toys and playing material—Questions 1, 4, 5, 6, 7, 8, 10, 11, and 15 in Figure 1. (A raw score of 1 or 2 on Questions 1, 4, 5 and 7—verbal and nonverbal communication, reaction when spoken to, and sharing of feelings—equals 1 point. For the remaining questions, a raw score of 1 equals 1 point. Other raw scores give no points.) An increased score after 1 year indicates that the child's communication abilities have increased (i.e., that the child communicates more eagerly and willingly). The maximum score is 9 points. The results for the two groups of children, registered before and after the experimental period, are presented in Figure 2.

Children in the control group had some higher and some lower scores after the experimental period, and nine of the children in the diet group had higher scores after 1 year. Mean results before and after the experimental period were, respectively, 3.9 ($SD = 0.9$) and 6.2 ($SD = 1.1$) for the diet group and 4.3 ($SD = 1.3$) and 4.5 ($SD = 1.6$) for the control group. For the diet group, the improvement was significant ($p < .007$, nonparametric two-tailed Wilcoxon test), but for the control group, it was insignificant. Significant differences in de-

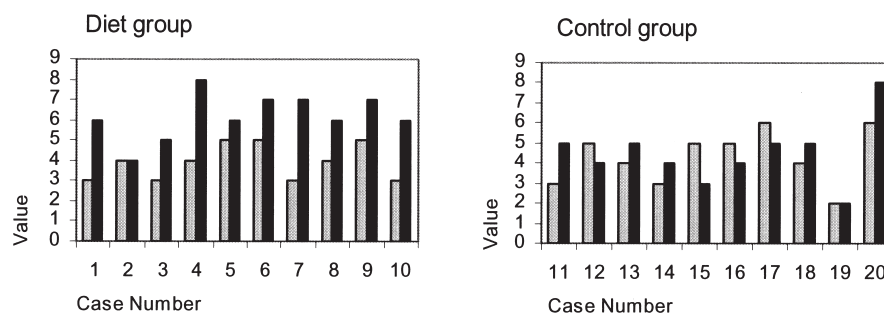


FIGURE 2. K-scores (communication and interaction) for the diet and the control group before (gray) and after (black) the experimental period. The higher the score, the more the child communicates and interacts. An increased score after 1 year indicates positive development.

velopment were found between the two groups ($p < .004$, nonparametric two-tailed Mann Whitney U test).

Resistance to communication and interaction ($M =$ scores) is computed from scores for verbal and nonverbal communication, reaction when spoken to, resistance to learning, sharing of feelings, reactions to physical contact, eye contact, and peer relationship—Questions 1, 4, 5, 6, 7, 8, 10, and 11 in Figure 1. (On each of these questions, a raw score of 3 or 4 equals 1 point. Other raw scores give no points.) The maximum score is 8 points. A decrease in score shows positive development—increased communication or willingness to interact and communicate. In Figure 3, the individual results of the children, registered before and after the experimental period of 1 year, are displayed.

In the diet group, resistance to communication and interaction had disappeared completely for 8 out of the 10 children during the experimental period. Mean results for the diet group were 2.5 ($SD = 1.0$) and 0.2 ($SD = 0.4$) before and after intervention, respectively; these results represent a significant reduction of resistance to communication ($p < .004$, nonparametric two-tailed Wilcoxon test). One child in the control group had none of these traits initially and still had none after 1 year. Means for the control group before and after the same period were, respectively, 2.3 ($SD = 1.7$) and 1.9 ($SD = 1.4$), an insignificant improvement. The development in the two groups was significantly different ($p < .004$, nonparametric two-tailed Mann Whitney U test).

Social interaction or isolation ($I =$ scores) is calculated from the questions related to resistance to communication and interaction and the questions related to abilities to interact and communicate. ($I\text{-score} = M\text{-score} - K\text{-score} + 9$). The result is an I -score, which describes a child's degree of withdrawal or aloofness, of 0 to 17. Deviant social interaction ranges from 4 to 17 points, and moderate to severe isolation starts at 8 points and increases with severity. The pre- and postregistration data and the I -score can be seen in Figure 4.

All but one child in the control group showed varying degrees of social isolation before the experiment started. Seven children on the diet were, after 1 year, communicating in a normal way and had an I -score of 3 or lower. The nine children in the control group that initially had problems in this area still had problems after 1 year. Mean results for the diet group before and after the experiment were, respectively, 7.6 ($SD = 1.7$) and 3.0 ($SD = 1.4$), a significant reduction of social isolation ($p < .005$, nonparametric two-tailed Wilcoxon test). For the control group, the mean results were 7.1 ($SD = 2.8$) and 6.2 ($SD = 2.9$), an insignificant reduction. A significant difference was found between the two

groups ($p < .003$, nonparametric two-tailed Mann Whitney U test).

The unusual or bizarre behavior score ($B =$ score) is composed by calculating compulsive or stereotypic communication, echolalia, adult dependency, strange emotional reactions, abnormal anxiety, reactions to changes in environment or routines, peculiar handling of toys and playing material, attachment/affinity for special items, and unusual movements or motor behavior—Questions 2, 3, 9, 12, 13, 14, 15, 16, and 17 in Figure 1. (For Questions 9, 13, and 14, a score of 3 or 4 equals 1 point. For the remaining questions, raw scores of 2, 3, or 4 equal 1 point. Other raw scores give no points.) A decrease in B -score is indicative of

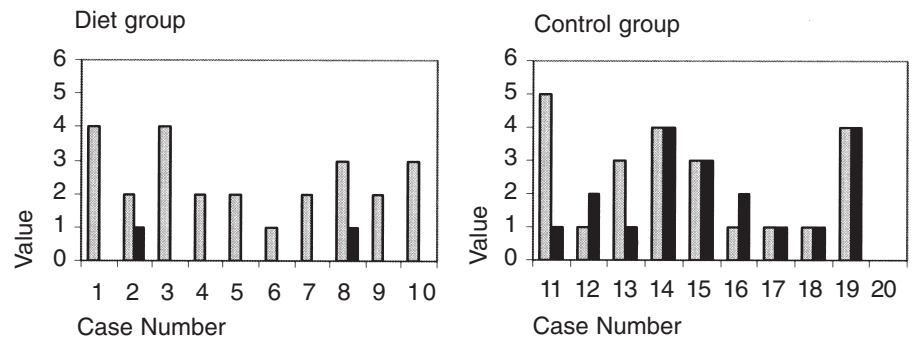


FIGURE 3. M-scores (resistance to communication and interaction) for the diet and the control group before (gray) and after (black) the experimental period. The higher the score, the more the child resists communication and interaction. A reduced score after 1 year indicates positive development.

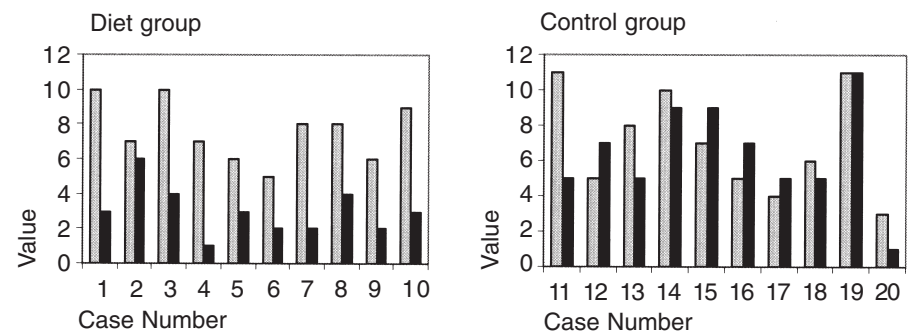


FIGURE 4. I-scores (social isolation) for the diet and the control group before (gray) and after (black) the experimental period. The higher the score, the more withdrawn the child is. A reduced score after 1 year indicates positive development, more interest in social contact and interaction. A score of 3 or less is typical for normally communicating children.

more normalized behavior, with a score of 2 points or lower considered normal. The individual results registered before and after 1 year can be seen from Figure 5.

After 1 year, a score of 2 points or lower was found for six of the children in the diet group and three of the children in the control group. The mean results for the diet group were 4.9 ($SD = 1.5$) before the diet and 2.6 ($SD = 1.7$) after the diet, a significant reduction of strange behavior ($p < .007$, nonparametric two-tailed Wilcoxon test). Before and after the experimental period, the control group had mean results of 4.5 ($SD = 1.6$) and 4.8 ($SD = 2.6$), respectively, an insignificant change. The difference between the groups was significant ($p < .007$, nonparametric two-tailed Mann Whitney U test).

An evaluation of total impairment of each child and of the two groups of children was conducted. The scores of social isolation and the scores of bizarre behavior before and after the experimental period were added. Calculations showed a significant decrease in the autistic behavior of individuals in the diet group, with a mean of 12.5 ($SD = 2.2$) before and 5.6 ($SD = 2.4$) after the dietary intervention ($p < .005$, nonparametric two-tailed Wilcoxon test). In the control group, the means were 11.5 ($SD = 3.9$) initially and 11.2 ($SD = 5.0$) after 1 year. The two groups' development was significantly different ($p < .001$, nonparametric two-tailed Mann Whitney U test). The total impairment of the individual children in the two groups can be seen in Figure 6.

Figure 6 illustrates that to a varying degree, these children's autistic traits

hampered their development before the experimental period. In the diet group, the lowest total impairment score was 10 and the highest 16. In the control group, the lowest score was 6 and the highest 16. After 1 year, the diet group's scores ranged from 2 to 9, and the control group's scores ranged from 1 to 17. In the diet group, a decrease in autistic behavior was registered for all the children, with scores varying from 2 to 10 points. In the control group, the picture was rather different. One child had a marked positive development, with a decrease of 7 to 1. A decrease was also registered for four other children, but the five remaining children had increased autistic behavior after the experimental period. The varying impairment of autistic behavior was also reflected in the 17 questions, with varying means for both the diet and the control group before the experimental period. This is illustrated in the Figures 7 and 8.

The statistical significance of the changes regarding each of the 17 questions related to autistic behavior was calculated. The means of all the questions decreased for the diet group during the intervention period, and significant changes were found for 12 of them after the experimental period was over ($p < .05$, nonparametric Wilcoxon two-tailed test). The questions for which significant changes were registered were on verbal communication (Question 1), compulsive or stereotypic communication (2), reaction when spoken to (5), resistance to learning (6), reactions to physical contact (8), eye contact (10), peer relationships (11), abnormal anxiety (13), reactions to changes in environment or routines (14), handling of toys and playing material (15), attachment/affinity for special items (16), and unusual movements or motor behavior (17). In the control group, some questions had a lower mean and some had a higher mean after 1 year. These changes were insignificant. With regard to the differences between the two groups of children, significant differences ($p < .05$, nonparametric two-tailed Mann Whitney U test) were found for verbal communication (1), reaction when spoken to (5), peer relationships

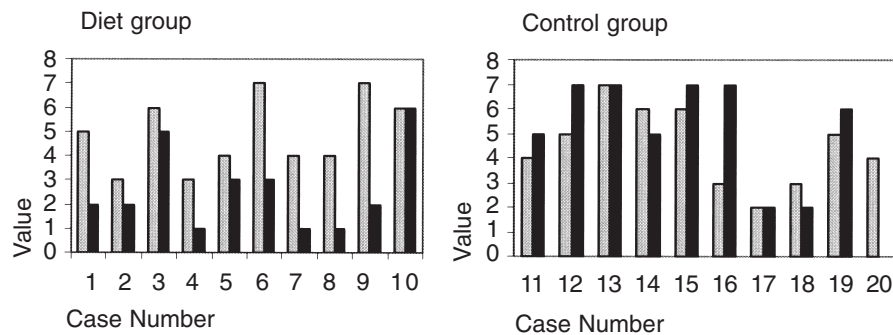


FIGURE 5. B-scores (bizarre or strange behavior) for the diet and the control group before (gray) and after (black) the experimental period. The higher the score, the more strange traits can be observed in the child's behavior. A reduced score after 1 year indicates a positive development, less strange behavior. A score of 2 or less is regarded as normal.

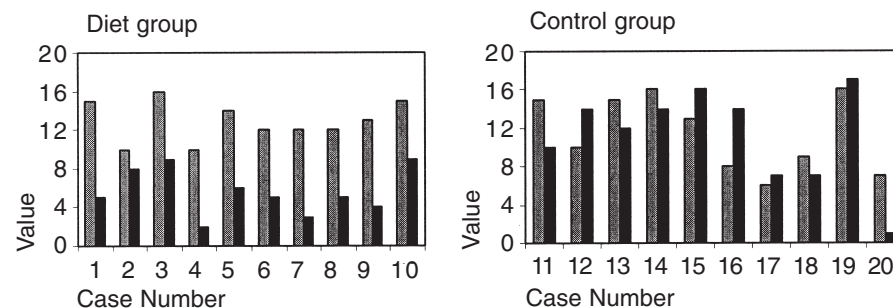


FIGURE 6. Total impairment scores, for both social isolation and bizarre behavior, for the diet and the control group before (gray) and after (black) the experimental period.

(11), abnormal anxiety (13), and reactions to changes in environment or routines (14).

The tests carried out before and after the experimental period (for detailed results for each child and for the groups, see Knivsberg et al., 2002) also showed that the children in the diet group did better than those in the control group. A significant increase ($p < .03$, nonparametric two-tailed Wilcoxon test) was found for the diet group on the cognitive test, and a significant decrease ($p < .05$, nonparametric two-tailed Wilcoxon test) was found for the control group. Linguistic age increased in both groups: The diet group had a mean increase of 12 months, and the control group had a mean increase of 9 months. Regarding motor impairment, the diet group experienced a small decrease, and the control group experienced a small increase. Significant differences between the groups were found with regard to development of cognitive abilities ($p < .004$, nonparametric two-tailed Mann Whitney U test) and motor skills ($p < .04$, nonparametric two-tailed Mann Whitney U test). Urine analyses were not conducted after the experimental period because we did not receive an adequate number of samples from each matched pair of participants.

Discussion

Structured special education is important to enhance development in children with autism (Gillberg, 1995; Wing, 1996). The question raised in this study was if children with autism would benefit from a diet free of the proteins gluten and casein. To our knowledge, this is the first study with diet and control groups participating for 1 year. Behavioral changes were marked and significant for the group of children randomly assigned to the diet group. The development for these children was better than the development for the children in the control group. The results support our hypothesis that the dietary intervention would have a positive effect and correspond with previously published reports on dietary interventions for individuals with

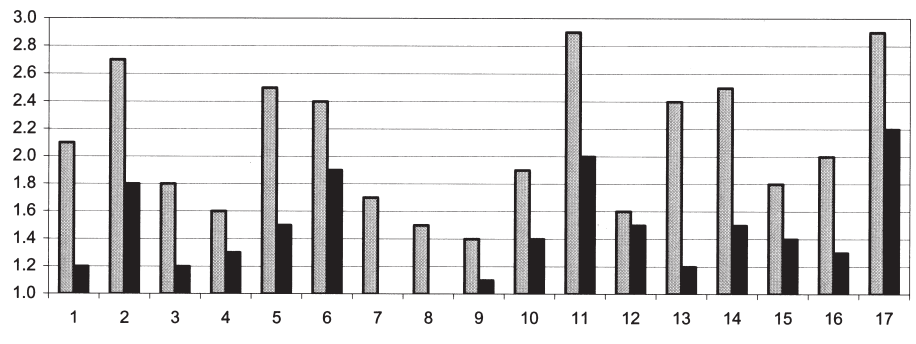


FIGURE 7. Mean of the 17 questions related to autistic behavior before (gray) and after (black) the experimental period for the diet group. Note. 1 = normal behavior, 4 = extremely deviant behavior.

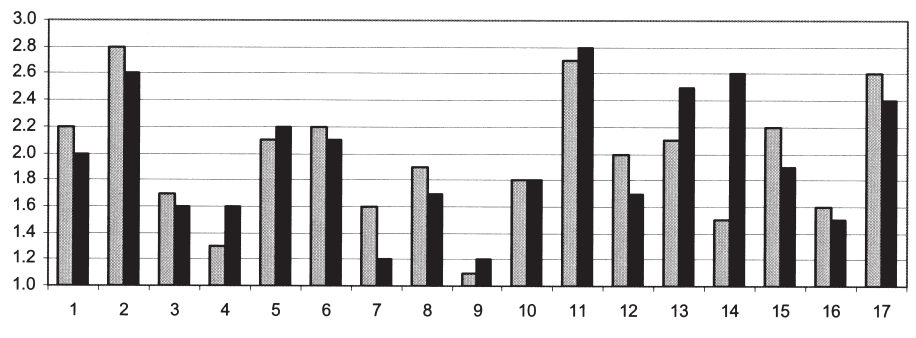


FIGURE 8. Mean of the 17 questions related to autistic behavior before (gray) and after (black) the experimental period for the control group. Note. 1 = normal behavior, 4 = extremely deviant behavior.

autism (Adams & Conn, 1997; Cade et al., 1999; Klaveness & Bigam, 2002; Knivsberg et al., 2002; Knivsberg et al., 1999; Knivsberg et al., 1995; Knivsberg et al., 1990; Lucarelli et al., 1995; K. L. Reichelt et al., 1990; Rimland, 1988; 2000; R. Shattock, 1995; Whiteley et al., 1999).

Current knowledge on the theoretical framework and support for dietary intervention has emerged from biomedical research in the same period that research on dietary intervention has been carried out. Review articles that describe the biomedical research in more detail have recently been published (P. Shattock & Whiteley, 2002; Wakefield et al., 2002). Wakefield et al. underlined the gut-brain connection, stating that neuroactive compounds can cross mucosa and the blood-brain barrier, which is not a new assumption but an accepted fact that is critical to knowledge of oral medica-

tion. They suggested that gastrointestinal pathology is involved in both autism and other developmental and behavioral disorders.

Regarding design, hypothetically, all the participants could have been on a diet during the entire experimental period. They could have been randomly assigned to a group that would receive gluten and casein in capsules or as powder, or to a group that would be given placebo capsules or powder. Theoretically, this would have been possible if the children had lived in an institution with strict control. All our participants lived at home. We doubt that parents would allow a diet to be carried out for a whole year, whether at home or in an institution, if no improvement was noted. The ethical aspect of such an experiment should also be considered.

One of the strengths of this study is that the children lived at home in differ-

ent parts of the country. The parents were not told the names of other participants, and to our knowledge there was no contact between the parents of children in either of the groups. Contact might have influenced expectations regarding the effect of the diet. Another strength is that the project leader did not know to which group each child had been assigned. Also, in a project of this kind, neutral observers could have followed the groups, but they would not have been unaware of the dieting aspect.

One limitation of this study is that monitoring of compliance with diet was not carried out. A very close follow-up by the dietician and urinary peptide analyses on regular intervals might have provided more information on this aspect. However, much contact and attention might have had unexpected influence on expectations. We tried to give both groups of parents attention through regular contact with trained special educators regardless of whether the child used diet or not. Also, we had planned to conduct urine analyses after 1 year, as we have previously done in an open study on dietary intervention (Knivsberg et al., 1995). This might have added extra value to the results. Due to circumstances beyond our control, however, this could not be accomplished.

When evaluating changes in children's behavior, it may be argued that it is difficult to decide whether changes are due to intervention or maturation. The autistic symptoms are differently expressed at different age levels, and they change over time (Wing, 1996). It is unlikely that significant changes would have occurred because of maturation in only one of the two participating groups in the study.

The placebo effect must also be considered. The assumption that the diet could have a positive effect might have altered the attitude of parents toward their children. This is a limitation that has to be taken into account in any intervention study. It seems questionable, though, that placebo effect could have affected all the parents and children in the same positive way for a whole year. Placebo effect would then have had to be active also in all previously reported studies.

Registration of the autistic behavior needed to be done as thoroughly as possible with data that could be operationalized. Our choice of standardized registration schemes in a Nordic language was limited, but we would most likely have chosen the DIPAB, even if we had had a wider choice of schemes. We also consider the *Leiter International Performance Scale* a good choice because it can be conducted without verbal communication and the child does not have to look at the test leader. Formal testing of these children is difficult and often stressful for the child. In this study, the testing was carried out in a familiar surrounding, with a significant, familiar adult present, and conducted during the time of the day when the child normally had his one-on-one training. Still, a number of variables might have influenced the test results (e.g., the mood of the child, a bad day, an upcoming flu). The teacher or assistant did convey, however, that the children's answers were what they expected.

The results clearly differed for the two groups of children. In the diet group, resistance to communication, social isolation, and strange behavior decreased significantly, whereas willingness and abilities to communicate increased significantly. Changes were also found for the control group, but they were insignificant. In the diet group, all the children changed in the same direction. For some, the positive development was substantial and for others it was not, but all of them had fewer autistic traits after 1 year. In the control group, five children had decreased and five had increased autistic behavior after 1 year. One child did remarkably well. According to P. Shattock and Savery (1997), autistic behavior normally fluctuates; good periods are followed by more difficult ones, and vice versa. In other words, the results registered for the control group are in accordance with what could be expected. The positive changes in the diet group are also underlined by the significant changes found for the specific items evaluated.

The present study demonstrated a reduction of autistic behaviour and an increase of communicative skills in the children in the diet group. Reduction of

autistic behavior and increase of communicative abilities enable children to learn in a more effective way. We consider the results of the study promising for the group of children with autism and urinary peptide abnormalities. We also consider the results encouraging for new studies that need to be conducted in this area of intervention.

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AUTHORS' NOTE

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